

## REMARKS

### 1. Preliminary Remarks

#### a. Status of the Claims

Claims 31 and 33-42 are pending in this application, and claims 34-42 have been withdrawn. Accordingly, claims 31 and 33 are under active consideration.

#### b. Declaration

At page 2, item 3 of the Office Action, the Examiner requires submission of a new declaration in compliance with 37 C.F.R. § 1.67(a). Applicant is still in the process of obtaining an inventor's declaration executed by inventor Jingwu Z. Zhang and will submit it under a supplemental response.

### 2. Patentability Remarks

At page 3, item 8 of the Office Action, the Examiner rejects claims 31 and 33 under 37 C.F.R. § 103(a) for allegedly being unpatentable over Zhang *et al.* (Science, 1993;261:1451-54; "Zhang '93" hereafter) in view of Zhang *et al.* (Crit. Rev. Immunol., 2001;21:41-55; "Zhang '01" hereafter), Tejada-Simon *et al.* (International Immunol., 2000;12(12):1651-50; "Tejada-Simon '00" hereafter) and WO 97/35879 ("Devaux" hereafter). The Examiner asserts that it would have been obvious to make a T cell vaccine as taught by Zhang '93 using T cells reactive to the MBP83-99 and MBP151-170 peptides taught by Zhang '01, plus T cells reactive with the PLP peptides taught by Tejada-Simon '00, and T cells reactive with the MOG peptides taught by Devaux, plus or minus T cells reactive with the MOG peptide taught by Tejada-Simon '00. The Examiner further asserts that one of skill in the art would have been motivated to do this in order to make a T cell vaccine that incorporates T cells that are reactive towards the immunodominant peptides from the MBP, PLP and MOG myelin proteins. Applicant respectfully disagrees, and submits that the cited references provide neither motivation nor expectation of success for arriving at the claimed subject matter.

The basis for Examiner's assertion of obviousness for the claimed subject matter is that one of skill would have been motivated to substitute the T cells of the vaccine taught by Zhang 93 with T cells reactive to two MBP peptides taught by Zhang '01, two PLP peptides taught by Tejada-Simon '00 and two MOG peptides taught by Devaux. The "simple substitution" basis for obviousness requires a finding that the results of the substitution would have been predictable. *See* MPEP § 2143.B. Additionally, the factual inquiry required for a finding of obviousness includes

ascertaining the differences between the claimed subject matter and the prior art, MPEP § 2141.II, which requires consideration of the prior art references as a whole. MPEP § 2141.02.

At the time that the instant application was filed, at least 123 peptides of MBP, 50 of PLP, and 67 of MOG were known. *See* Appendices A-C. These peptides are disclosed in the references cited by the Examiner, and in those submitted in the Information Disclosure Statement submitted herewith. These references all fail to specifically teach or suggest making a T cell vaccine with T cells that are reactive to exactly six myelin protein epitopes, let alone two specific peptides from MBP, two specific peptides from PLP, and two specific peptides from MOG. One of skill could have chosen to make a T cell vaccine with T cells reactive to 1 or 2 or 3, *etc.* peptides, up to the maximum number of peptides known for each myelin protein. For example, given the 123 known peptides of MBP, one of skill could have chosen to use any one of the 123, or any two of the 123, or any three of the 123, *etc.*, up to using all 123 known peptides for making a vaccine. Consequently, there were  $1.1 \times 10^{37}$  different combinations of MBP peptides,  $1.1 \times 10^{15}$  PLP peptides, and  $1.5 \times 10^{20}$  MOG peptides to choose from in order to make a T cell vaccine.<sup>1</sup> All told, given the number of possible peptide combinations for each of MBP, PLP, and MOG, there were at least  $1.7 \times 10^{72}$  different combinations of different numbers and kinds of peptides from MBP, PLP, and MOG from which one of skill could have chosen.<sup>2</sup>

As described above, the prior art gives no guidance to one of skill to produce the instantly claimed T cell vaccine. The Examiner admits that Zhang '93 does not teach or suggest using any of the peptides having instant SEQ ID NOs: 1-6. Office Action at p. 3. The Examiner likewise admits that Tejada-Simon '00 does not teach or suggest the specific peptide reactivity of the instantly claimed T cell vaccine. *See* Office Action at p. 4. The Examiner also admits that Devaux teaches MOG peptides "that are useful in compositions of the invention for treating MS." Office Action at p. 4. Thus, Devaux does not at all teach or suggest making a T cell vaccine or using one to treat MS, which is the subject matter of the instant claims. Nor does Devaux provide motivation to one of skill to make a T cell vaccine that is reactive to MOG peptides. Instead, Devaux discloses using MOG peptides themselves as an immunoreactive treatment against MS. *See, e.g.*, Devaux at claims 48-93.

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<sup>1</sup> This was calculated by using the formula  $n!/k!(n-k)!$ , where  $n$  is the number of possible peptides that may be selected, and  $k$  is the number of peptides actually selected. This calculation was performed for selecting from 1 up to the total number of known peptides for each myelin protein (*i.e.*, MBP, PLP, and MOG), and then added.

<sup>2</sup> This was calculated by multiplying the number of possible MBP, PLP, and MOG peptide combinations, respectively.

Nevertheless, even if one of skill were motivated to use peptides taught by Devaux to make a T cell vaccine, one of skill would not have the motivation or expectation of success for making the specific T cell vaccine of the instant claims—which is reactive to two specific peptides each of MBP, PLP, and MOG—from the greater than  $1.7 \times 10^{72}$  unique combinations of peptides known at the time of filing the instant application. Devaux does not teach or suggest using only the two specific MOG peptides to which the instantly claimed T cell vaccine is reactive, but rather discloses at least 46 MOG peptides. Furthermore, Applicant notes that Devaux does not teach using only immunodominant MOG peptides, and thus that if one of skill were motivated to make a T cell vaccine using T cells reactive to immunodominant peptides, Devaux provides little guidance as to which, if any, MOG peptides to use. Accordingly, none of the cited references provides motivation or expectation of success to one of skill for arriving at the T cell vaccine of claim 1 with specific reactivity to two particular peptides each of MBP, PLP, and MOG from the infinite number of possible peptide combinations known in the art at the time of filing. In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 103(a).

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

POLSINELLI SHUGHART PC

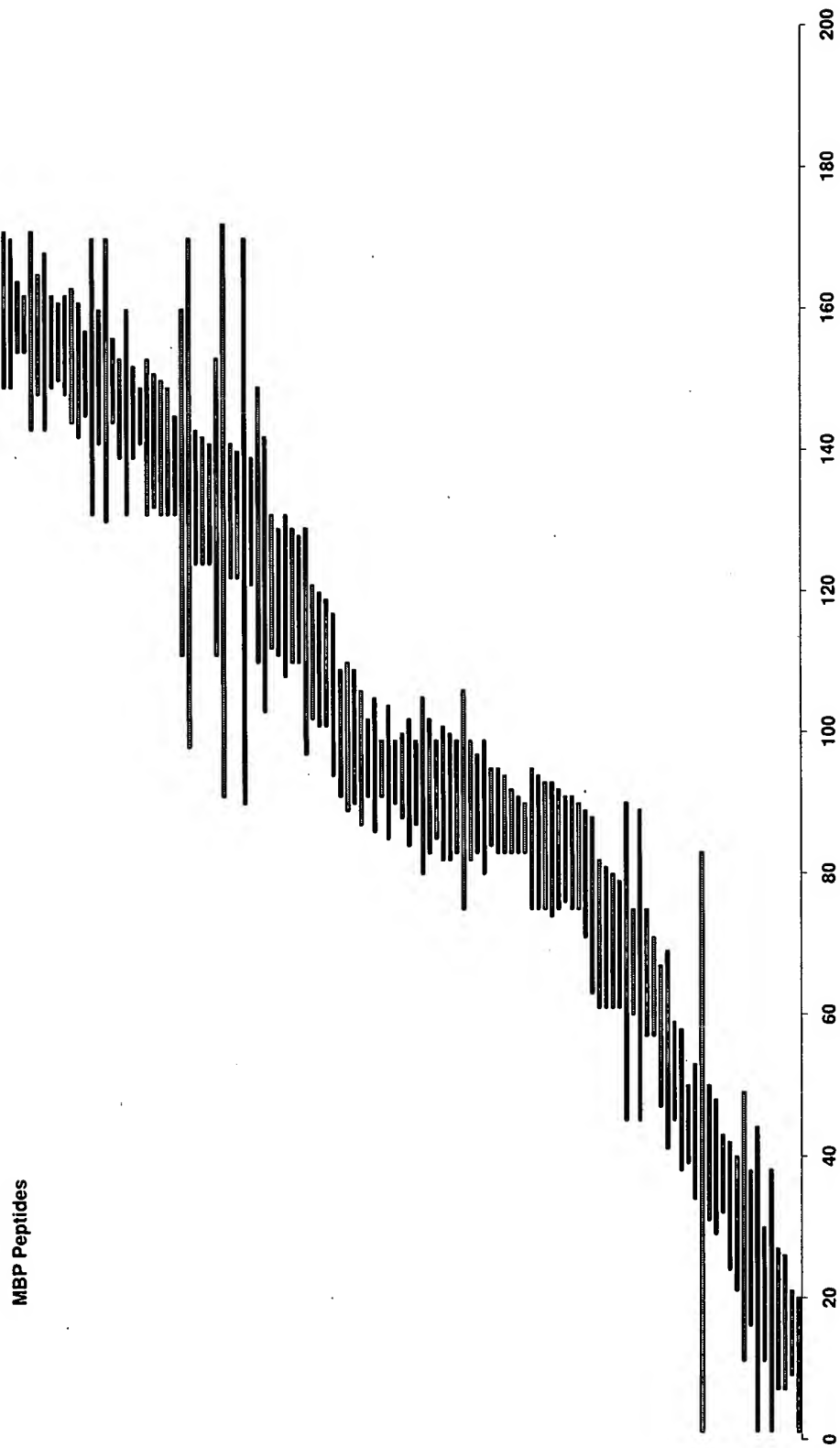
Dated: March 24, 2009

On behalf of: Teddy C. Scott, Jr., Ph.D.  
Registration No. 53,573

By: /Ron Galant, Ph.D./  
Ron Galant, Ph.D.  
Registration No. 60,558  
Customer No. 27148

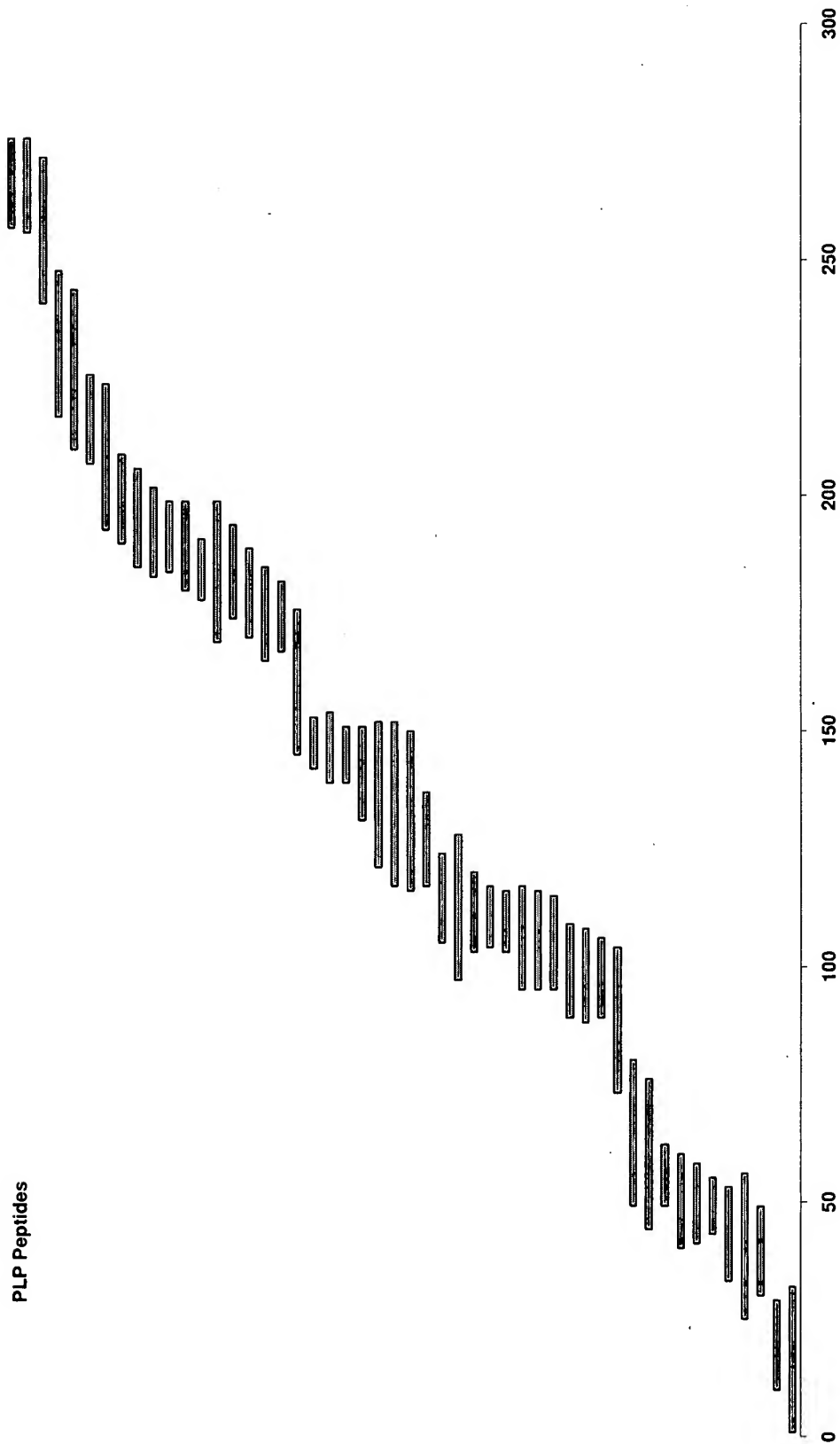
POLSINELLI SHUGHART PC  
180 N. Stetson Ave., Suite 4525  
Chicago, IL 60601  
312.819.1900 (main)  
312.819.2913 (E-fax)  
312.873.3613 (direct)

## APPENDIX A



## APPENDIX B

PLP Peptides



# APPENDIX C

MOG Peptides

